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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LEFFERS JR. GERALD G

ART UNIT PAPER NUMBER

1636

DATE MAILED: 12/03/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/843,150

Applicant(s)

CHAMBON, ET AL.

Examiner

Gerald G Leffers Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24, 26-46 and 49-52 is/are pending in the application.
- 4a) Of the above claim(s) 26-46 and 49-52 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of Group I (claims 1-24) in Paper No. 8 is acknowledged. The traversal is on the ground(s) that there is no undue search burden for the examiner to examine all of the groups together. This argument ignores the different classifications set forth in the restriction requirement for the different groups. A showing of a different classification is in itself sufficient to demonstrate a burdensome search requirement for combining the claims of the different groups. Alternatively, the argument does not acknowledge a different non-patent literature search required for the different inventions claimed in the different groups. It is noted that applicants have cited the guidelines for rejoinder of product and process of use claims as per *In re Ochiai*, and that claims 33-34 and 41-46 should be rejoined with the claims of Group I when the DNA and vector claims are found to be allowable. Upon indication that the DNA and vector claims are allowable, these claims will be rejoined.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-24, 26-46, 49-52 are pending in this application, with claims 26-46, 49-52 withdrawn from consideration as being directed to nonelected inventions.

Specification

The disclosure is objected to because of the following informalities: wherever sequence identifiers appear in the specification the format is incorrect (e.g. "SEQ ID N° 1) in claim 11). In each instance, it would be remedial to amend the sequence identifier to read "SEQ ID NO: ". This is particularly relevant for claim 11.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-13 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the claims is drawn towards a “variants” of a given polypeptide (e.g. a recombinase such as Cre or reporter proteins such as yellow fluorescent protein). The term “variant” is not explicitly defined in the specification. Read broadly, the term encompasses any possible amino acid variation of the protein that may retain the functional activity associated with the “wildtype” protein. Thus, the claim limitation of a “variant” of the recited proteins encompasses an extremely broad genus of proteins that must retain functional activity in the context of the claim.

The specification does not provide a structural/functional basis for one of skill in the art to envision altered embodiments of the recited polypeptides (i.e. variants) that retain functional activity. The prior art does not provide a sufficient number of specific embodiments of altered versions of the recited proteins to enable one of skill in the art to reasonably predict the structure of versions of the recited proteins that retain functional activity. In fact, the art of teaches the

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relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science, 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, one of skill in the art cannot reliably predict the structural/functional characteristics of a protein based upon primary sequence alone.

Given the lack of a basis in the instant specification or prior art for one of skill in the art to envision altered versions of the recited proteins that retain functional activity, and given the unpredictability in the art of predicting protein structural/functional characteristics based on primary sequence alone, one of skill in the art would not have been able to envision a sufficient number of specific "variants" of the recited proteins that retain functional activity to describe the broadly claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 1 is vague and indefinite in that the metes and bounds of the phrase "...in an opposite orientation..." are unclear. It is unclear in relations to what other structural feature of the claimed nucleic acid are the L1 or L2 sequences in opposite orientation. It appears from reading the specification that it would be remedial to insert in each case (i.e. either L1 or L2) the words "to one another" following the recited phrase.

Likewise, the metes and bounds of the phrase "...sequences A and B are in an opposite direction..." in claim 5 are unclear. Upon reading the specification, it appears it would be remedial to amend the claim language to clearly indicate that the sequences of A and B are oriented in an opposite direction from one another.

Claim 6 is vague and indefinite in that it is unclear how the L1 and L2 sequences can be the same, when claim 1 recites the limitation that the L1 and L2 sequences cannot recombine with one another.

Claim 8 is vague and indefinite in that the metes and bounds of the phrase "...wherein the site specific recombinase targeting sequence are selected from the group of site-specific recombinases composed of..." are unclear. The phrase is unclear in that it appears to specify that a targeting sequence (i.e. nucleotide sequence) is selected from a group of proteins. Also, the claim does not clearly indicate that the different proteins are to be selected in the alternative to one another. It is further noted the claim does not use proper Markush group language (i.e. selected from the group consisting of...and...) and is grammatically incorrect (i.e. sequence are selected). It would be remedial to amend the claim language to include proper Markush language to indicate that the targeting sequence is selected from a group of different recombinase recognition sequences (i.e. SSRTS).

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Claim 10 is vague and indefinite in that it uses terms for which it is unclear whether the term is open or closed claim language. These terms include the words "group composed of" and "harboring". It is suggested that the words "group consisting of" and "comprising" be utilized in place, respectively, of the cited terms.

Claims 9 and 12 recite the limitation of "natural or synthetic variants" of a given protein. Claims 8 and 22 recite the limitation of a "variant" of a given protein. It is unclear how different a protein can be from a recited protein and be considered a "variant" of that protein. It is also unclear how one would distinguish a priori what constitutes a "natural" variant versus a "synthetic" variant.

Claims 16-17 are vague and indefinite in that they appear to recite a Markush group where the members of the group include overlapping genres, or species of a genus within the same Markush group. For example, in claim 16 specifies a Markush group comprising a polypeptide, a protein and protein fragments. Protein fragments are themselves either proteins or polypeptides, or both. Claim 17 recites a Markush group comprising a reporter protein, a selection marker and protein of interest. Certainly, a selection marker or reporter protein qualify as a protein of interest.

Conclusion


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
December 2, 2002